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Severe COVID-19 infection associated with endothelial activation

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Mounting evidence supports the strong prognostic importance of D-dimers and the impact of coagulopathy in COVID-19 patients[1,2,3]. We would like to emphasize the significance of anticoagulation in severe COVID-19 disease, by adding our observation of highly pathological data on anti-phospholipid-antibodies, von Willebrand Factor (VWF) and Factor VIII. We observed a 72-year-old previously healthy male patient admitted to our hospital 6 days after the onset of respiratory symptoms and fever. Six days after admission, following a rapid deterioration of his clinical condition with development of acute respiratory distress syndrome, acute renal insufficiency and altered mental status, he was transferred to the intensive care unit (ICU). Supportive care with intubation, positive pressure ventilation and renal replacement therapy led to a stabilization of his condition. During the ICU stay, a continual increase of D-dimers was observed, from initially 0.69 mg/L to 2.55 mg/L on day 4, 2.81 mg/L on day 11 to 20.63 mg/L on day 21. At this time, IgG anti-cardiolipin antibodies (ACA) and anti-beta2-glycoprotein I (anti-β2-GPI) were negative, but IgM ACA elevated at 121.9 CU (normal <20 CU) and IgM anti-β2-GPI elevated at 275.3 CU (normal <20 CU). Furthermore, on day 21, we also observed a concurrent massive elevation of VWF, with VWF:antigen 555% (normal 42-136%) and VWF:activity 520% (normal 42-168%), accompanied by an increase of Factor VIII clotting activity of 369% (normal 55-164%). The increased VWF points towards massive endothelial stimulation and damage with release of VWF from Weibel-

Palade bodies. Interestingly, endothelial cells express ACE2, the receptor for SARS-CoV-2, thus possibly mediating endothelial activation[3]. The patient received prophylactic anticoagulation with dalteparin 5000 U s.c. daily from admission to hospital. We increased the dose to therapeutic anticoagulation with unfractionated heparin on day 21, without hemorrhagic complication. Since then, the patient is steadily improving, ventilation and hemodialysis could be successfully withdrawn, and he has been transferred from the ICU to a general ward. D-dimers decreased to 6.26 mg/L on day 24 and to 1.94 mg/L on day 29. Considering the high levels of VWF and factor VIII, we strongly suggest administering higher, possibly therapeutic doses of anticoagulation to these patients. The role of antiphospholipid antibodies, VWF and FVIII needs further study.

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